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Glaucoma Disease-Specific Adherence Measurement Tools Validated for Measuring Adherence to Glaucoma Medications: A Systematic Review

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ABSTRACT

Background: Reviewing validated glaucoma disease-specific tools for measuring adherence could encourage adherence monitoring to avoid progressive visual field losses in people living with glaucoma.

Aim: To review the literature on validated disease-specific tools for measuring adherence to glaucoma medications.

Methods: Relevant peer-reviewed publications from the year 2000 to 2022 from PubMed, EMBASE, Scopus, and PROquest were retrieved. For each search conducted, the name of the search engine used, date of search, number of publications retrieved, and keywords used were documented. The selected articles were reviewed for inclusion and assessed for biases and quality. Each tool was described by the type of measurement, technique for measurement, strengths and weaknesses, and method of validation, respectively.

Results: Out of the 10 included articles, seven glaucoma disease-specific tools were identified namely; Glaucoma Treatment Compliance Assessment Tool-Short form (GTCAT-S), Glaucoma Treatment Compliance Assessment Tool-Long form (GTCAT-L), Travatan Dosing Aid (TDA), Eye-Drop Satisfaction Questionnaire (EDSQ), Glaucoma Adherence Questionnaire-Revised (GAQ-R), Glaucoma Adherence Questionnaire-Old (GAQ-O), and Schwartz Adherence Questionnaire (SAQ). Three studies had a low risk of bias, and seven recorded a moderate risk of bias. The TDA, GTCAT-S, and GTCAT-L were rated as high-quality tools.

Conclusions: Seven glaucoma disease-specific tools for measuring adherence were found. Integration of regular measurement of medication adherence as part of care for glaucoma patients would be beneficial for both patients and providers of eye care.

1 | Introduction

Globally, glaucoma remains a significant sight-threatening disease with public health and economic implications [1]. It is the second leading cause of irreversible blindness globally and is characterized by optic neuropathies and raised intraocular pressure (IOP) [1, 2]. In automated visual field examination, the diseases is marked by specific structural findings in the optic disk together with functional defects [2]. About 60% of the nerve fibers are damaged before the appearance of defects in visual fields in most eyes with glaucoma [3]. Compared to those in developed countries, people living with glaucoma in developing countries have a higher risk of becoming blind as a result of progressive optic nerve degeneration due to nonadherence to medication [4, 5].

The use of ocular hypotensive medications plays a significant role in the control of IOP in glaucomatous eyes [6–10]. Adherence to these medications is therefore crucial in the management of the disease. Adherence to medication is the extent to which the medication-taking behavior of a patient corresponds with recommendations from the doctor [11]. Nonadherent patients are known to experience progressive reduction in their visual capabilities leading to low quality of life in general [12–14].

Prevalence of nonadherence to medication among patients with glaucoma is reported to range from 5% to 80%, with differences in methodologies used accounting for this variation [12, 15].

Several tools have been developed for measuring patients' adherence to medication. These tools may be classified as objective, subjective, direct, or indirect tools, respectively [16]. Subjective tools refer to the assessment of the medication-taking behavior of patients with the help of a validated questionnaire [16]. The objective form of measuring adherence involves the use of medication dose counts, pharmacy records, and electronic monitoring systems [16]. The direct tools relate to the use of biological markers or metabolite levels or concentrations which may indicate an intake of medication by the patient [16]. The indirect tools may refer to the use of both subjective and objective tools for adherence measurement [16].

The use of validated glaucoma disease-specific tools may be more sensitive in revealing significant changes in the eye health of people living with glaucoma compared to generic tools. Such tools may also be the preferred choice of the patient as they focus specifically on their ocular health.

Considering the health implications and economic burden of nonadherence to glaucoma medications, it is imperative to conduct a systematic review of glaucoma disease-specific tools for measuring adherence to glaucoma medications. Reviewing these validated tools could promote adherence monitoring which may help in improving patient safety by lowering medication-related harm to improve patient outcomes through application of targeted treatments [17]. Also, monitoring of adherence reduces healthcare costs and avoidable hospital stays [18]. Additionally, it improves the patient–provider relationship and informs the need for treatment adjustment or alternative therapies where possible [19].

This review will identify evidence-based validated glaucoma disease-specific medication adherence measurement tools to augment the management of glaucoma. The review may assist clinicians and researchers in selecting validated glaucoma disease-specific tools for measuring adherence to glaucoma medication.

2 | Methods

2.1 | Search Strategy

This systematic review examined relevant peer-reviewed articles published from the year 2000 to 2022 in electronic databases such as, PubMed, EMBASE, Scopus, and ProQuest. Starting this review from the year 2000 is justified by the facts that, some research before year 2000 may be outdated or less relevant to current practice as research methods have improved significantly since year 2000 with changes in guidelines and policies and focus on contemporary issues.

Names of the search engines used, date of search, number of publications retrieved, and keywords used were all recorded. Selected articles were screened and reviewed for inclusion. Titles, names of authors, year of article publication, and other related variables were examined manually to remove duplicates. The principal investigator (PI) together with other authors independently reviewed each article for inclusion. Uncertainties were resolved through consensus in the selection of the articles. The "PICO" (Population, Intervention, Comparison/Control and Outcome) framework with an addition of a time frame factor (T) was used in structuring the review process (Table 1).

2.2 | The Research Question

The research question for this review was: "what are the validated glaucoma disease-specific tools for measuring adherence to glaucoma medications"?

The PICOT methodology was used to define the research question above. We did not include a comparison in our PICOT framework as our objective was to update readers on glaucoma disease-specific tools for measuring adherence to glaucoma medications. We, therefore, had no intention of comparing the tools to a gold standard. A schematic presentation of the framework is illustrated in Table 1 below.

2.3 | Search Filters

We refined our search strategy by using search filters for study design, measurement, and language. These filters included; "Randomized Controlled Trial (RCT)," "Observational Study," "Cohort Study," "Cross-Sectional Study," "Questionnaire," "Survey," "Scale," and "English."

2.4 | Inclusion and Exclusion Criteria

The review included only peer-reviewed articles published in English language between the years 2000 and 2022. Peer-reviewed articles published in other languages, and non-peer-reviewed publications, gray literature including reports, working papers, government documents, white papers, and studies which were not conducted within the period under consideration were excluded. Figure 1 illustrates the flowchart of the study selection.

2.5 | Main Outcome Measure

The main outcome measure was an update on glaucoma disease-specific tools for measuring adherence to glaucoma medications.

TABLE 1 | Population, intervention, comparison, outcome, and time (PICOT) framework.

PICO	Description	Search terms and connectors (OR and AND)
Population	Validated tools/scales/questionnaire/survey/ instrument/models/device/items for measuring nonadherence.	Validated* OR tools*, validated* OR scales*, validate* OR questionnaire*, validated* OR survey*, validated* OR instrument*, validated* OR models*, validated OR device, validated OR items. Validated* AND tools*, validated* AND scales*, validate* AND questionnaire*, validated* AND survey*, validated* AND instrument*, validated* AND models*, validated AND device, validated AND items.
Intervention/ impact	Measurement of nonadherence.	Measurement* OR nonadherence*, measurement* OR nonadherence*, measurement* OR adherence*, measurement* OR compliance*, measurement* OR noncompliance*, measurement* OR persistence*. Measurement* AND nonadherence*, measurement* AND nonadherence*, measurement* AND adherence*, measurement* AND compliance*, measurement* AND noncompliance*, measurement* AND persistence*.
Comparison	—	—
Outcome	Update on glaucoma disease-specific tools for measuring adherence to glaucoma medications.	Glaucoma* OR medication nonadherence measurement*, glaucoma* OR medication adherence measurement*, glaucoma* OR compliance measurement*, glaucoma* OR noncompliance measurement*. Glaucoma* AND medication nonadherence measurement*, glaucoma* AND medication adherence measurement*, glaucoma* AND compliance measurement*, glaucoma* AND noncompliance measurement*.
Time	Specific time frame for the study.	Year 2000 to 2022.

2.6 | Data Extraction and Quality Analysis

Studies that met the inclusion criteria were considered for data extraction and analysis. The extracted papers were assessed considering the general characteristics of the studies, risk of bias, the level of quality of the tools, and the classification of the tools by the type of measurement, technique for measurement, strength and weakness, and what is measured by the tool.

2.6.1 | General Characteristics of the Studies

The general characteristics of the selected studies included the study objectives, the study design, the glaucoma disease-specific tool, the disease condition, the study setting, the study duration (months), the country, and the reported limitations of the study.

2.6.2 | Risk of Bias Assessment for Selected Articles

Selection, performance, detection, and information biases were evaluated using the Cochrane Collaboration Risk of Bias assessment tool [21].

The Cochrane Collaboration Risk of Bias assessment tool was adapted for this review to assess bias [21]. This was done by modifying the tool by the removal of the domains specific to RCTs, retaining relevant domains, and adding domains relevant to non-RCT designs such as selection bias.

2.6.3 | Quality Criteria

An assessment of the quality of the tools was done using a methodology developed by a group of international ophthalmologists from 23 countries across the globe [22]. This methodology had eight quality parameters which included pre-study hypothesis, intended population, item identification and selection, scoring, validity, sensitivity, responsiveness, and ease of use. The quality of the tools was assessed as high (3), medium (2), low (1), and not reported (0). The total scores were then aggregated for each method to determine the level of quality of the tool. Tools with a total score from 0 to 8, 9 to 16, and 17 to 24 were described as low quality, medium quality, and high-quality, respectively. A summary of the assessment is presented on Figure 2 below.

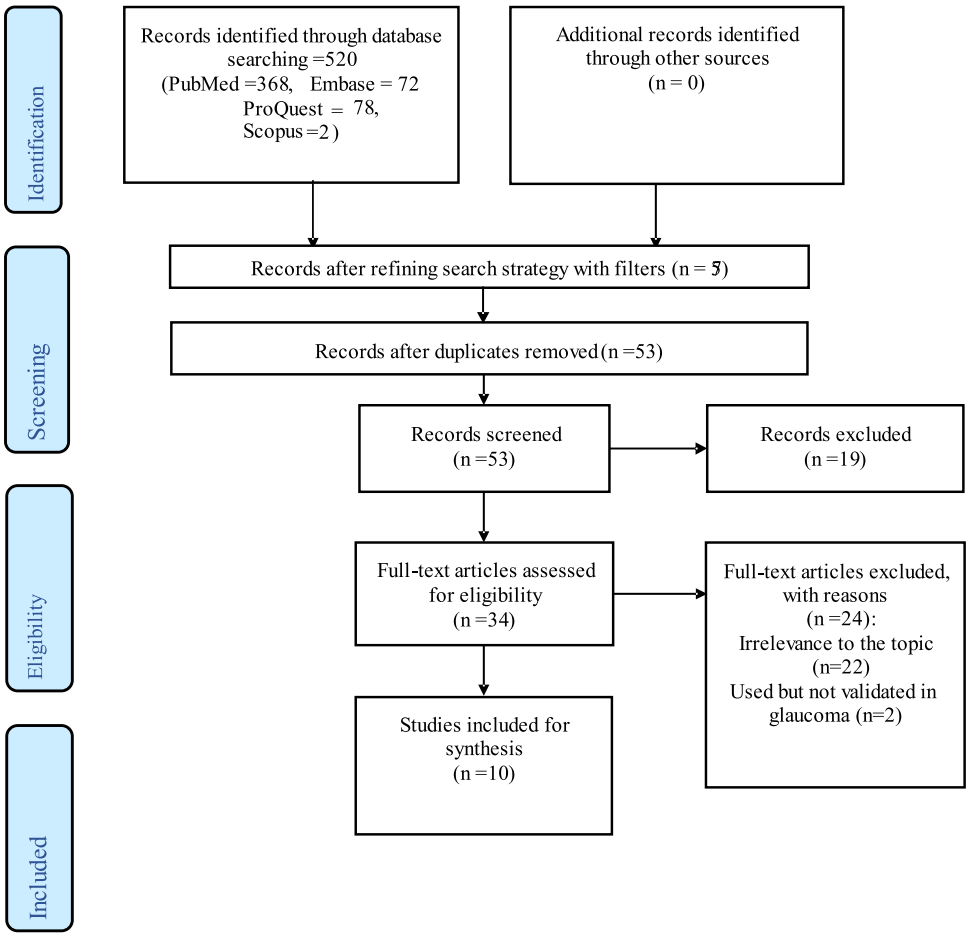

FIGURE 1 | PRISMA flowchart of the study selection [20].

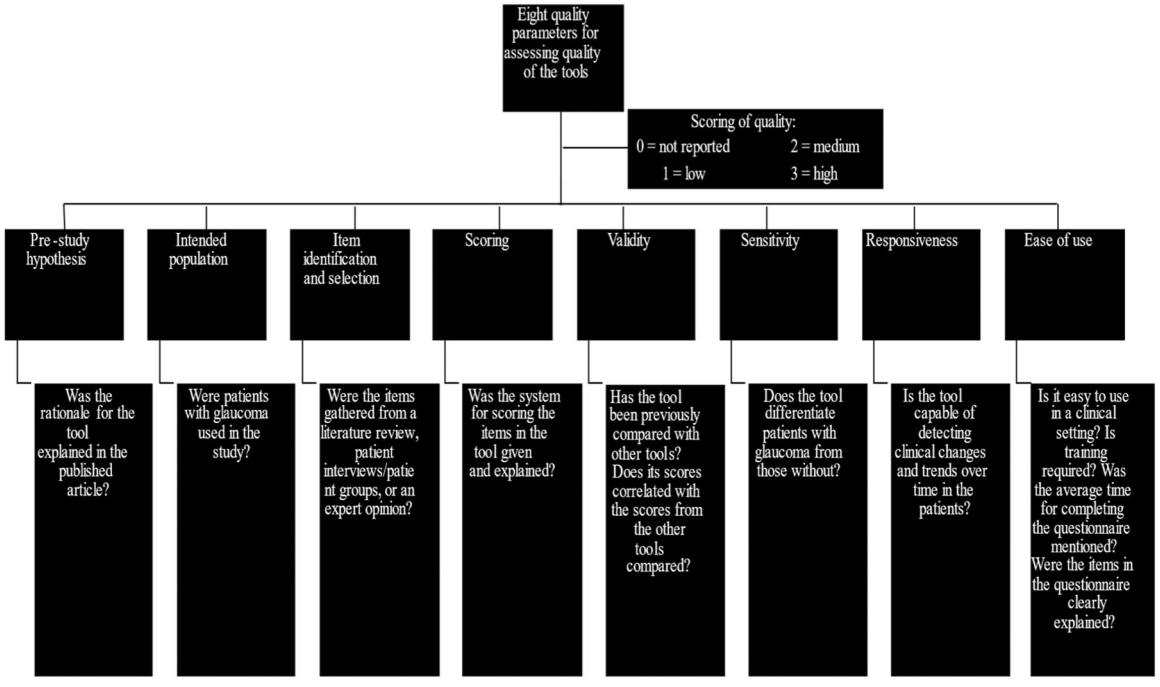

FIGURE 2 | Quality criteria for assessing glaucoma disease-specific tools for adherence measurement.

2.6.4 | Classification of Glaucoma Disease-Specific Tools for Measuring Adherence to Glaucoma Medication

Additionally, an assessment of each of the tools was done in terms of the strengths and weakness of the tools, the type of measurement, that is either objective or subjective tools, the technique for measurement, that is either direct or indirect tool, what the tool measures, and the method of validation.

2.7 | Registration of Review

This review has been registered in the PROSPERO database for systematic reviews with registration number; PROSPERO 2021 CRD42021272092.

3 | Results

3.1 | Identification of Glaucoma Disease-Specific Tools for Measuring Adherence

A total of 520 records were identified through database searching. Three-hundred and sixty-eight articles were identified in PubMed, 78 in ProQuest, 72 in Embase, and two in Scopus. After refining the search strategy with search filters, a total of 75 articles were identified. After screening and removal of duplicates, 34 articles were left as full-text articles for eligibility assessment. Eligibility assessment was done and 24 articles were excluded with the reasons being; 22 articles were not relevant to the topic and two articles were not validated among glaucoma patients.

Ten studies were finally included for qualitative synthesis after a full-text review. Figure 1 shows a PRISMA flowchart of the study selection.

Of the 10 selected articles, seven glaucoma disease-specific tools for measuring adherence in glaucoma patients were identified namely; Glaucoma Treatment Compliance Assessment Tool-Short form (GTCAT-S), Glaucoma Treatment Compliance Assessment Tool-Long form (GTCAT-L), Travatan Dosing Aid (TDA), Eye-Drop Satisfaction Questionnaire (EDSQ), Glaucoma Adherence Questionnaire-Revised (GAQ-R), Glaucoma Adherence Questionnaire-Old (GAQ-O), and Schwartz Adherence Questionnaire (SAQ) (Table 2).

3.2 | General Characteristics of the Selected Articles

Of the 10 studies analyzed, there were two each of cross-sectional studies, mixed methods, and observational case series with repeated measures, and one each of RCT, cohort study, psychometric analysis, and qualitative exploratory study, respectively.

All of the studies were hospital-based and explored glaucoma. Four studies were conducted in the United States of America, three in the United Kingdom, and two each were done in Brazil and France. The study duration ranged from 1 month to 12 months. Key findings are summarized in Table 2.

3.3 | Risk of Bias Assessment

Three studies had a low risk of bias, whiles seven studies recorded a moderate risk of bias (Table 3).

3.4 | Quality Level of the Tools

The TDA, GTCAT-S, and GTCAT-L had high-quality scores, respectively. The other tools recorded medium-quality scores (Table 4).

3.5 | Classification of the Tools by Strength, Weakness, What Is Measured, and Method of Validation

All the seven tools identified were indirect and noninvasive techniques. The TDA was the only objective tool and the rest were subjective (observer-reported or patient-reported) tools. The classification of the tools by strength, weakness, what is measured, and method of validation are presented on Table 5.

4 | Discussion

Making the best use of glaucoma medications is important to eye health professionals and patients in view of the rising cost of investments in new drug development and treatment regimens [1]. After decades of research on glaucoma medication adherence, there is still inadequate guidance for eye health professionals and researchers in the choice of the most suitable tool for measuring adherence to glaucoma medications [16]. We, therefore, conducted a systematic review to update clinicians and researchers with disease-specific tools for measuring adherence to glaucoma medications. To the best of our knowledge, this is the first systematic review of disease-specific tools for measuring adherence to glaucoma medications. Seven glaucoma disease-specific tools namely; the GTCAT-S, GTCAT-L, TDA, EDSQ, GAQ-R, GAQ-O, and SAQ were identified.

An evaluation of these tools using quality criteria by Gazzard et al. [22] revealed the TDA, GTCAT-S and GTCAT-L as high-quality tools and the others as medium-quality tools. The low risk of bias in our selected studies explains the use of valid approaches in the selection of study participants, prevention of bias, and analysis of data in the selected studies. The low-risk studies recorded the least bias with results considered valid. The moderate risk studies had some level of bias but were not so significant to invalidate the results of the studies. The use of critical appraisal methods is essential in assessing the strengths and weaknesses of studies included in systematic reviews [33].

The tools identified may be classified as subjective or objective tools and as direct or indirect tools [16]. Our findings reveal that all the tools reviewed were subjective, except the TDA which is

TABLE 2 | General characteristics of included studies.

Number	Authors/year of publication	Study design	Glaucoma disease-specific tool	Sample size	Duration of study (months)	Country where the study was conducted	Key findings	Limitations reported about the study
1	Cronin et al. [23]/2007	Descriptive cross-sectional study.	TDA	87 drops	6	USA	On average, the TDA delivered 99% of the drug.	Failure to fully depress the TDA lever or prolongation of lever depression could potentially underestimate patient compliance.
2	Barker and Mansberger [24] /2019	Prospective observational case series with repeated measures.	GTCAT-S	183	2	USA	The 27 statements predicted adherence.	Hawthorne effect. Outcome may be different in patients with different severities of glaucoma. Other predictors of adherence such as health literacy were not included.
3	Mansberger et al. [25]/2013	Cross-sectional study design with focus groups and a prospective observational case series with repeated measures (mixed methods).	GTCAT-L	78	3	USA	The GTCAT shows excellent repeatability, content, construct, and predictive validity for glaucoma adherence.	Participants were recruited from a single center. Medications were given free of charge to participants. Hawthorne effect.
4	Abe et al. [26]/2018	Prospective, observational cohort study.	GTCAT-S	7	1	Brazil	The Portuguese-translated version of the GTCAT showed acceptable psychometric properties.	Hawthorne effect.
5	Barker et al. [27]/2015	Psychometric analysis.	GTCAT-L	201	1	Brazil	GTCAT showed acceptable psychometric properties.	Hawthorne effect.
6	Nordmann et al. [28]/2007	A qualitative exploratory study.	EDSQ	15	1	UK, France	The EDSQ could be used to evaluate patient satisfaction and compliance with eye-drop treatment.	Absence of saturation as interview methodology. Possible bias could have been introduced in translating French into English before analysis.

(Continues)

TABLE 2 | (Continued)

Number	Authors/year of publication	Study design	Glaucoma disease-specific tool	Sample size	Duration of study (months)	Country where the study was conducted	Key findings	Limitations reported about the study
7	Gray et al. [29]/2010	Observational cross-sectional study.	GAQ-Old version	138	4	UK	Although important, knowledge alone may not sufficiently improve adherence.	Limited by its cross-sectional nature. Time constraints for the recruitment period. Participant numbers were small for some of the analyses. Recall bias.
8	Gray et al. [30]/2012	A two-arm, single-masked exploratory randomized controlled trial.	GAQ- Revised version	127	12	UK	Modeling patient care according to healthcare needs and beliefs about illness and medicines can have a significant impact on improving adherence.	Of the intervention-arm patients who did not receive the intervention in full, 90% did not collect adequate prescriptions to maintain continuous therapy and 60% demonstrated poor clinical outcomes at 24 months. These patients either withdrew from the study or were difficult to contact.
9	Schwartz et al. [31]/2009	A qualitative exploratory and observational cross-sectional study (mixed method).	SAQ	202	Not stated	USA	Number of adherence problems and adherence scores were similar in both populations.	Inclusion of only those who kept a follow-up appointment. Participants may not be representative of the wider population of glaucoma patients.
10	Regnault et al. [32]/2010	An observational, multicenter, cross-sectional, and retrospective study (mixed method).	EDSQ	184	1.5	France	The EDSQ had a satisfactory psychometric property and a promising relationship to compliance profiles.	Small sample size. Travalert is limited to Travatan and DuoTrav and therefore extrapolation to other products would need additional data collection.

Abbreviations: EDSQ, eye-drop satisfaction questionnaire; GAQ-O, glaucoma adherence questionnaire-old version; GAQ-R, glaucoma adherence questionnaire-revised version; GTCAT-L, glaucoma treatment compliance assessment tool-long form; SAQ, Schwartz adherence questionnaire; TDA, Travatan dosing aid; UK, United Kingdom; USA, United State of America.

TABLE 3 | Quality of reviewed articles.

Number	Author	Title	Performance bias	Information bias	Selection bias	Detection bias	Total score	Interpretation
1	Cronin et al. [23]	Accuracy and performance of a commercially available dosing aid.	1	1	0	0	2	Moderate risk of bias
2	Barker and Mansberger [24]	Psychometric properties of the reduced version of the glaucoma treatment compliance assessment tool (GTCAT).	1	1	1	1	4	Low risk of bias
3	Mansberger et al. [25]	Psychometrics of a new questionnaire to assess glaucoma adherence: The glaucoma treatment compliance assessment tool.	0	1	1	0	2	Moderate risk of bias
4	Abe et al. [26]	Psychometric properties of the glaucoma treatment compliance assessment tool (GTCAT) in a Brazilian population.	1	1	1	0	3	Low risk of bias
5	Barker et al. [27]	Psychometric properties of the glaucoma treatment compliance assessment tool in a multicentre trial.	1	1	0	1	3	Low risk of bias
6	Nordmann et al. [28]	Development of the conceptual framework for the Eye-Drop Satisfaction Questionnaire (EDSQ) in glaucoma using a qualitative study.	1	0	0	0	1	Moderate risk of bias
7	Gray et al. [29]	Preliminary survey of educational support for patients prescribed ocular hypotensive therapy.	1	0	0	0	1	Moderate risk of bias
8	Gray et al. [30]	Individualized patient care as an adjunct to standard care for promoting adherence to ocular hypotensive therapy: An exploratory randomized controlled trial.	1	0	0	0	1	Moderate risk of bias

(Continues)

TABLE 3 | (Continued)

Number	Author	Title	Performance bias	Information bias	Selection bias	Detection bias	Total score	Interpretation
9	Schwartz et al. [31]	An assessment of readiness for behavior changes in patients prescribed ocular hypotensive therapy.	1	0	0	0	1	Moderate risk of bias
10	Regnault et al. [32]	Scoring and psychometric properties of the Eye Drop Satisfaction Questionnaire (EDSQ), an instrument to assess satisfaction and compliance with glaucoma treatment.	1	0	0	0	1	Moderate risk of bias

Note: A score of −1 = showing a high risk of bias; 0 = unclear risk of bias; +1 = low risk of bias. A total score from −4 to 0 = high risk of bias; 1 to 2 = moderate risk of bias; and 3 to 4 = low risk of bias.

an objective tool. Since none of the tools involve the use of biological markers or metabolite levels or concentrations that could suggest a patient is taking medicine, none of the techniques could be categorized as a direct tool [16]. Direct tools are highly acurate, less prone to bias, and provide real-time information [16]. They are, however, costly, invasive, and have limited assessability [16].

All the seven tools identified are indirect tools since they assess adherence through proxy measurements or patient-reported outcomes, rather than directly observing medication intake through biological markers or metabolic concentration. Indirect tools could therefore be either subjective or objective tools [16]. The indirect tools which are subjective are cost-effective, easy to use, widely available, and provide insight into patient medication intake behavior [16]. However, they are subject to bias, depend on data quality, and have limited generalizability [16].

All the tools were developed through rigorous validation processes that demonstrated significant reliability and validity. As a subjective tool, the GTCAT-L (a 47-statement questionnaire) assesses multiple behavioral factors associated with glaucoma medication adherence [25]. Its development was based on the Health Belief Model which explains that a person with a condition such as glaucoma is more likely to adhere to medication if he or she places a high value on the current state of vision and also believes that the use of glaucoma medications would prevent further visual deterioration [34, 35]. Several studies have demonstrated the efficacy of the model in predicting health behaviors [36–39]. The GTCAT-L was validated using regression and factor analysis to ensure its relevance and comprehensiveness [25]. The validation of the GTCAT-L demonstrated an excellent content, construct, and predictive validity respectively, with an excellent reliability [25]. Notable studies reporting the use of the GTCAT-L include; Barker et al. [27] and El-Sakhy and El-Rahman Mohamed [40].

The GTCAT-S (27-statement questionnaire) [24] is the reduced version of the GTCAT-L with more robust construct validity compared to the GTCAT-L [25]. Shorter-length questionnaires are known to improve response rate, predictive, and construct validity [41, 42]. Validation of the tool in the Portuguese language in Brazil showed an acceptable test−retest reliability and internal consistency [26]. The validation utilized principal component analysis (CPA) to reduce the original 47-statement GTCAT-L to 27 statements and assessed predictive and construct validity using multiple logistic regression analysis and CPA with the Health Belief Model [24, 26]. Studies such as Cho et al. [43] and Sanchez et al. [44] have used the GTCAT-S in assessing adherence.

The EDSQ is made up of 46 items, assessing six domains of medication adherence namely; patient characteristics, treatment characteristics, patient−clinician relationship, patient experience, patient-treatment interaction, and patient knowledge about glaucoma [32]. It was developed through a qualitative interview of 15 French and English patients with glaucoma [28]. The EDSQ was validated by cognitive debriefing, expert review, factor analysis, internal consistency, and criterion validity [32]. Additionally, regression analysis was used to predict adherence based on the EDSQ scores [32]. The tool proved

TABLE 4 | Quality score for the tools.

Number	Quality parameters	Guidance	Tool Score GTCAT-S [24, 26]	GTCAT-L [25, 27]	TDA [23]	EDSQ [28, 32]	GAQ-O [29]	GAQ-R [30]	SAQ [31]
1	Pre-study hypothesis	Is the rationale of the questionnaire explained (here or in former publications)?	3	3	3	3	2	2	2
2	Intended population	Are patients with glaucoma involved? If no, what is the other population? Is this studied/intended population relevant versus patients with glaucoma?	3	3	3	3	3	3	3
3	Item identification and selection	Were items collected from: Literature review? Patient interviews/patient groups? Expert opinion? Was the pilot questionnaire tested (rash or factor analysis, statistical justification of final items)? Are the items clinically relevant to the target population?	3	3	3	3	3	3	3
4	Scoring	Is there a description of the different parameters and of how the questionnaire should be scored?	3	3	3	2	2	2	2
5	Validity	Was the questionnaire previously compared with another (or other measurements)? If yes, did the questionnaire correlate with the scores of the other questionnaire/ measurements?	3	3	3	2	2	2	2
6	Sensitivity	Is the questionnaire able to discriminate patients with glaucoma from a	2	2	3	1	1	1	1

(Continues)

TABLE 4 | (Continued)

Number	Quality parameters	Guidance	Tool Score GTCAT-S [24, 26]	GTCAT-L [25, 27]	TDA [23]	EDSQ [28, 32]	GAQ-O [29]	GAQ-R [30]	SAQ [31]
		nonglaucoma patient? Different stages and severity of the disease?							
7	Responsiveness	Is the questionnaire able to detect clinical changes and trends over time?	2	1	3	1	1	2	1
8	Ease of use	Is the questionnaire easy to administer/fill-in for the patient? (Training needed, time to fill-in, clear items, etc.)	2	1	2	1	1	1	1
Total score (out of 24)			**21**	**19**	**23**	16	15	16	15
Interpretation of quality			**High quality**	**High quality**	**High quality**	Medium quality	Medium quality	Medium quality	Medium quality

Note: Scoring of the quality parameters: 3 = high quality; 2 = medium quality; 1 = low quality; and 0 = not reported. Total scores of the quality of the tools: 0 to 8 = low quality; 9 to 16 = medium quality; and 17 to 24 = high quality. Tools appearing in bold are high quality.

Abbreviations: EDSQ, eye-drop satisfaction questionnaire; GAQ-O, glaucoma adherence questionnaire-old version; GAQ-R, glaucoma adherence questionnaire-revised version; GTCAT-L, glaucoma treatment compliance assessment tool-long form; SAQ, Schwartz adherence questionnaire; TDA, Travatan dosing aid.

TABLE 5 | Classification of the tools by strength, weakness, what is measured, and method of validation.

Tool	Description	Strength	Weakness	What is measured	Method of validation
Objective tool					
TDA [23]	**An electronic medication dosing tool designed to hold a bottle of travoprost with an attached base which records the time and day when the lever that administers the medication is fully depressed.**	1. **Noninvasive.** 2. **Accurate.** 3. **Objective.** 4. **Gives detailed information on adherence level.**	1. **Patients are aware of the measurement (possible Hawthorne effects).** 2. **May only be available for certain medications.** 3. **Not a viable long-term option.** 4. **It is expensive.** 5. **There may be no clear indication that the drop is being instilled.**	**An overall percentage of drop doses instilled.**	**Validated by comparative analysis with TDA recordings compared to patient self-reports. Correlation analysis was then done to assess agreement between TDA and Medication Event Monitoring System (MEMS). Sensitivity and specificity analysis was done to evaluate TDA's accuracy. High accuracy with 93% agreement between TDA and MEMS. Strong reliability, ICC = 0.92. Improved adherence, 25% increase in adherence rate.**
Subjective tools					
GTCAT-S [24]	**It is a 27-statement questionnaire that assesses multiple behavioral factors associated with glaucoma medication adherence. It is the reduced version of the GTCAT-L.**	1. **Noninvasive.** 2. **Easy to use.** 3. **Inexpensive.** 4. **Less time to complete.**	1. **May be affected by reporting bias.** 2. **May overestimate adherence.** 3. **May be subjective.**	**A value interpreted according to an established standard of cut-off level.**	**Principal component analysis (CPA) was used to remove statements that did not load, reducing the original 47-statement GTCAT to a 27-statement version. Multiple logistic regression analysis was used to assess predictive validity. Construct validity was assessed using the PCA, extracting five components of the Health Belief Model (knowledge, susceptibility, cues-to-action, self-efficacy, and barriers).**
GTCAT-L [25]	**It is a 47-statement questionnaire that assesses multiple behavioral factors**	1. **Noninvasive.** 2. **Easy to use.**	1. **Affected by reporting bias.**	**A value interpreted according to an**	**Validated through content validity index (CVI) to ensure tool relevance and**

(Continues)

TABLE 5 | (Continued)

Tool	Description	Strength	Weakness	What is measured	Method of validation
	associated with glaucoma medication adherence.	3. **Inexpensive.**	2. **Overestimate adherence.** 3. **Subjective.** 4. **Takes more time to complete.**	**established standard of cut-off level.**	**comprehensiveness. Factor analysis was then used to confirm underlying constructs. Internal consistency yielded a Cronbach's Alpha ($\alpha = 0.83$). Criterion validity recorded a correlation, $r = 0.65$. Regression analysis predicted adherence based on GTCAT-Long scores.**
EDSQ32	It is made up of 46 items, assessing six domains; patient characteristics, treatment characteristics, patient−clinician relationship, patient experience, patient-treatment interaction, and patient knowledge about glaucoma.	1. Noninvasive. 2. Easy to use. 3. Inexpensive.	1. May be affected by reporting bias. 2. May overestimate adherence. 3. May be subjective. 4. May take more time to complete.	A value interpreted according to an established standard of cut-off level.	Validated by cognitive debriefing to ensured respondent understanding. Expert review was done to confirmed content relevance. Factor analysis was done to identify underlying constructs. Internal consistency was assessed which yielded a Cronbach's Alpha of $\alpha = 0.85$. Criterion validity yielded a Pearson's correlation of $r = 0.70$. Regression analysis was used to predict adherence based on EDSQ scores to identify nonadherent patients.
GAQ-O [29]	A 42-item self-report questionnaire developed by literature review and discussions with experts in questionnaire development and ophthalmology.	1. Noninvasive. 2. Easy to use. 3. Inexpensive.	1. May be affected by reporting bias. 2. May overestimate adherence. 3. May be subjective. 4. Takes more time to complete.	A value interpreted according to an established standard of cut-off level.	Validated through expert panel reviews to confirm content relevance. Cognitive debriefing was done to ensure respondent understanding. Factor analysis followed to identify underlying constructs. Internal consistency was assessed ($\alpha = 0.81$) and criterion validity yielded, $r = 0.65$. Regression analysis predicted adherence based on the GAQ scores.

(Continues)

TABLE 5 | (Continued)

Tool	Description	Strength	Weakness	What is measured	Method of validation
GAQ-R [30]	This is the revised version of the GAQ-O. It is a 39-item questionnaire with questions about glaucoma knowledge, intentional and non-intentional drop omission, social status, co-morbidity, support, and lifestyle factors affecting adherence.	1. Noninvasive. 2. Easy to use. 3. Inexpensive. 4. Less time to complete.	1. May be affected by reporting bias. 2. May overestimate adherence. 3. May be subjective.	A value interpreted according to an established standard of cut-off level.	Validated by factor analysis to confirm underlying constructs. Internal consistency yielded $\alpha = 0.85$. Intraclass correlation coefficient (ICC) was used to evaluate test−retest reliability (ICC = 0.83). Criterion validity yielded $r = 0.72$. Regression analysis predicted adherence based on GAQ-R scores. Rasch analysis evaluated item response theory (IRT) properties which detected changes in adherence over time.
SAQ [31]	This is a 62-item, self-administered questionnaire based on the transtheoretical model of change. Questions included; demographics, health and medications, use of/problems with medications, and visual function.	1. Noninvasive. 2. Easy to use. 3. Inexpensive.	1. May be affected by reporting bias. 2. May overestimate adherence. 3. May be Subjective. 4. Takes more time to complete.	A value interpreted according to an established standard of cut-off level.	Validated by expert panel reviews to confirm content relevance. Cognitive debriefing was done to ensure respondent understand the process. Factor analysis was done to identify underlying constructs. Internal consistency yielded an $\alpha = 0.87$ and criterion validity recorded, $r = 0.75$. Regression analysis predicted adherence based on SAQ scores to identify nonadherent patients.

Note: Tools appearing in bold are high quality.

Abbreviations: EDSQ, eye-drop satisfaction questionnaire; GAQ-O, glaucoma adherence questionnaire-old version; GAQ-R, glaucoma adherence questionnaire-revised version; GTCAT-L, glaucoma treatment compliance assessment tool-long form; SAQ, Schwartz adherence questionnaire; TDA, Travatan dosing aid.

to be internally consistent and reliable with good construct validity [32]. Few studies have used this tool in assessing adherence to glaucoma medications [32, 45].

The original form of the GAQ (GAQ-O) is a 42-item tool developed through a review of available literature and discussions by experts in the development of patient-reported outcome measures (PROMs) in ophthalmology [29]. Its domains include; information on social status, knowledge of glaucoma, difficulties in managing eye drops due to other medical conditions or lifestyle, the support patients received for instilling drops, and adherence status [29]. Its content and face validity were confirmed by the expert group and piloted among 50 patients [29]. Thus, the validation of the GAQ-O was carried out through expert panel review, cognitive debriefing, factor analysis, internal consistency assessment, and criterion validation. Regression analysis was further used in predicting adherence based on GAQ scores [29].

To improve the GAQ-O, a 39-item questionnaire (GAQ-R) was developed [30]. Questions about glaucoma knowledge, intentional and non-intentional drop omission, social status, comorbidity, support, and lifestyle factors affecting adherence were included [30]. GAQ-R was also validated through factor analysis, internal consistency, test−retest reliability, criterion validity, regression analysis, and item response theory properties [30]. The GAQ-R may take lesser time to complete compared to the GAQ-O [30]. Studies such as Gray et al. [30] have used this tool to evaluate the impact of individualized patient care, as an adjunct to standard care.

The SAQ is a 62-item tool developed based on the transtheoretical model of change [31]. The questions in this tool include; demographics, health and medications, use of/problems with medications, and visual function [31]. These questions were derived from a review of ophthalmic and non-ophthalmic literature and modified and validated by a panel of nine glaucoma specialists and behavioral and health economics experts [31]. The SAQ was validated through an expert panel review to confirm content relevance and cognitive debriefing to ensure understanding. Factor analysis was further employed to identify underlying constructs, internal consistency, and criterion validity. Additionally, regression analysis was used to predict adherence based on SAQ scores [31].

Subjective tools such as GTCAT-L/S, GAQ-O/R, SAQ, and EDSQ, have components capable of identifying barriers to medication adherence, assessing adherence behaviors and evaluating self-administration, eye drop satisfaction, and knowledge and belief about glaucoma [24–32].

Subjective tools are mainly self-reported tools which could be distributed online and administered as structured interviews or written questionnaires [16, 46]. They are noninvasive, easy-to-use, inexpensive, accommodate different disease conditions, and give real-time feedback [47, 48]. These tools can easily be adapted and validated in different patient populations and may be useful in providing additional information about barriers to adherence, attitudes, behaviors, beliefs, and intentions of patients about medications. Some studies have reported the overestimation of adherence among patients using subjective tools compared to objective tools due to recall or reporting bias by patients [16, 46, 49]. Most of these tools take more time to administer and may be affected by the communication skills of the interviewer [16, 46].

The TDA, as an objective tool has an electronic drug monitor and a medication event monitoring system (MEMS) that holds for only travoprost medication [23]. A bottle of travoprost is usually placed in the device and a lever is used to administer a drop. It has a built-in memory chip which records the time and date each time the lever is depressed. It can only provide data on the use of travoprost because the device was not designed to accommodate other medication bottles. In the validation of the TDA, a high accuracy and reliability was established with a 25% increase in adherence rate, after correlating the TDA data with patient self-report data [23].

The TDA has widely been used in the validation of self-reported tools, although not a gold standard by consensus from the scientific community involved in adherence measurements [43, 46, 50–55]. The use of MEMS has been found to closely correlate with the clinical effectiveness of several interventions in clinical studies [56–58].

Compared to subjective tools, objective tools are highly accurate and usually used as a standard for validating other tools. They are known to be noninvasive, accurate, and give detailed information on adherence levels. They give precise and detailed information about the number of doses taken and other deviations from the dosing regimen [16, 23]. With objective tools such as the TDA, improper use of the device and opening the container without taking the medication may contribute to incorrect outcomes. The use of objective tools in large populations is limited by the relatively high price of the device, as well as some practical issues like potential complications that may arise with refilling the prescription in the local pharmacy or some medication preparations [16, 23]. Objective tools may, however, be expensive and currently not reimbursable by most medical insurance agencies [23]. Patients may be aware of the measurement (Hawthorne effects) which could bias the outcome measure [16]. Objective tools may only be available for certain medications, and there may not be any clear indication that the drop is being instilled [16]. They may also have technical issues such as battery life challenges and device malfunction [16].

This review has demonstrated the significance of using glaucoma disease-specific adherence tools in identifying non-adherent patients and has provided guidance for eye care professionals in the choice of tools for measuring adherence to glaucoma medication. Understanding the similarities and differences between these tools could assist healthcare providers and researchers in choosing the most suitable tool for their clinical needs and studies. However, there is currently no single tool capable of meeting all the needs of end-users, as each tool has its inherent weaknesses.

The implications of these findings to clinical practice and research is that the choice of a particular tool should be based on; the objective of the measurement, the ease of use of the tool in a clinical setting, the cost-effectiveness of the tool, accuracy

in assessing adherence, sensitivity in providing information on possible barriers to adherence, and the ability to identify small changes in the ocular health of patients. Integrating regular adherence measurement in the management of glaucoma is essential in assessing the impact of prescribed eye medications on the ocular health of patients with glaucoma. Thus, these tools could clinically serve as important endpoint measures for evaluating treatment efficacy and interpreting clinical outcomes such as IOP levels and visual field defects. Adherence measurement could, therefore, serve as a key element in treatment decision-making.

The combination of two or more tools is recommended as it offers better, more accurate and additional information on the ocular health of patients with glaucoma.

The strength of this review is that it used four electronic databases, sensitive search filters and the PRISMA statement. However, its limitation is the inclusion of only English-language full-text articles, overlooking articles in other foreign-language articles that could have also yielded some positive outcomes.

5 | Conclusions

Seven validated glaucoma disease-specific tools for measuring adherence were found namely; the GTCAT-S, GTCAT-L, TDA, EDSQ, GAQ-R, GAQ-O, and SAQ. By understanding the characterists of these tools, eye care professionals and researchers can select the best tool for their patients' needs and studies respectively. There is, therefore, a need to develop more glaucoma disease-specific adherence measuring tools to ensure optimal care and management of patients with glaucoma. There is also a need for eye care providers to integrate the measurement of medication adherence as part of their regular care for glaucoma patients.

Author Contributions

B. Abaidoo: conceptualization, investigation, funding acquisition, writing–original draft, writing–review and editing, visualization, validation, methodology, software, formal analysis, project administration, data curation, resources. **K. P. Mashige:** conceptualization, methodology, writing–review and editing, supervision, investigation. **P. Govender-Poonsamy:** supervision, methodology, conceptualization, investigation, writing–review, and editing. **N. N. Tagoe:** methodology, writing–review and editing. **V. A. Essuman:** methodology, writing–review and editing. **S. Y. Adam:** methodology, writing–review and editing.

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Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

Data for this article is available upon reasonable request through the corresponding author.

Transparency Statement

The lead author, B. Abaidoo, affirms that this manuscript is an honest, accurate, and transparent account of the study being reported, that no important aspects of the study have been omitted, and that any discrepancies from the study as planned (and if relevant, registered) have been explained.

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